



# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE  
United States Patent and Trademark Office  
Address: COMMISSIONER FOR PATENTS  
P.O. Box 1450  
Alexandria, Virginia 22313-1450  
www.uspto.gov

| APPLICATION NO.   | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|-------------|----------------------|---------------------|------------------|
| 09/926,218  | 01/28/2002  | Arne Holmgren        | P21480              | 8453             |
| 7055  | 7590        | 11/10/2004           | EXAMINER            |                  |
| GREENBLUM & BERNSTEIN, P.L.C.<br>1950 ROLAND CLARKE PLACE<br>RESTON, VA 20191 |             |                      | KUMAR, SHAILENDRA   |                  |
|   |             |                      | ART UNIT            | PAPER NUMBER     |
|   |             |                      | 1621                |                  |

DATE MAILED: 11/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.



UNITED STATES PATENT AND TRADEMARK OFFICE

---

COMMISSIONER FOR PATENTS  
UNITED STATES PATENT AND TRADEMARK OFFICE  
P.O. Box 1450  
ALEXANDRIA, VA 22313-1450  
[www.uspto.gov](http://www.uspto.gov)

**BEFORE THE BOARD OF PATENT APPEALS  
AND INTERFERENCES**

Application Number: 09/926,218  
Filing Date: January 28, 2002  
Appellant(s): HOLMGREN ET AL.

---

Bruce H. Bernstein  
For Appellant

**EXAMINER'S ANSWER**

This is in response to the appeal brief filed 8/24/2004.

**(1) *Real Party in Interest***

A statement identifying the real party in interest is contained in the brief.

**(2) *Related Appeals and Interferences***

A statement identifying the related appeals and interferences which will directly affect or be directly affected by or have a bearing on the decision in the pending appeal is contained in the brief.

**(3) *Status of Claims***

The statement of the status of the claims contained in the brief is correct.

**(4) *Status of Amendments After Final***

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

The amendment after final rejection filed on 4/28/04 has been entered.

**(5) *Summary of Invention***

The summary of invention contained in the brief is correct.

**(6) *Issues***

The appellant's statement of the issues in the brief is correct.

**(7) *Grouping of Claims***

Appellant's brief includes a statement that claims 13-25 do not stand or fall together and provides reasons as set forth in 37 CFR 1.192(c)(7) and (c)(8).

**(8) *Claims Appealed***

The copy of the appealed claims contained in the Appendix to the brief is correct.

**(9) Prior Art of Record**

Arteel, G.E., "Function of Thioredoxin reductase as a Peroxynitrite Reductase Using Selenocystine or Ebselen" Chem. Res. Toxicol, vol 12, (1999) pp 264-269

Muller, A. "A novel Biologically Active Seleno-organic Compound-I" Biochemical Pharmacology, Vol 33, no. 30(1984), pp 3235-3239

**(10) Grounds of Rejection**

The following ground(s) of rejection are applicable to the appealed claims:

1. Claims 13-25 are rejected under 35 U.S.C. 102(b) as being anticipated by Arteel et al (Chem. Res. Toxicol., 1999).

Instant claims are directed to a method for reduction of a substrate with thioredoxin reductase, by combining the thioredoxin reductase, the substrate, and NADPH, so as to reduce the substrate, and wherein the substrate is Ebselene. Claims 15 and 18 are directed to a method of enhancing peroxidase activity of thioredoxin reductase, using the substrate, NADPH and thioredoxin reductase. Claim 17 is directed to a method of oxidizing reduced thioredoxin by Ebselene. Claim 19 is directed to a method of preventing peroxidation of a substance by combining thioredoxin, thioredoxin reductase, NADPH and Ebselene. Claims 21 and 22 are directed to above methods in mammals.

Arteel et al is teaching a substrate for thioredoxin reductase which has the same formula as claimed herein, see the title, wherein Ebselen is mentioned. This is same as the 2-phenyl-1,2-benzisoselenazol-3(2H). See line 1 of the abstract, wherein mammal is

Art Unit: 1621

cited, column 1, 2<sup>nd</sup> paragraph, lines 1-3 and 7-8, column 2, 1<sup>st</sup> paragraph on page 264, teach all the elements of the instant claims.

2. Claims 13-25 are rejected under 35 U.S.C. 103(a) as being unpatentable over combined teachings of Arteel et al and Muller et al.

Instant claims are directed to an enhancer of the peroxidase activity of thioredoxin reductase, which comprises a substance selected from formula (1) and (1') of claim 1.

Arteel has been described supra. In brief, the reference is teaching a substrate for thioredoxin reductase which is the same as claimed herein. The difference between the reference and herein claimed subject matter is that the reference is not teaching that the same substrate is also an enhancer of the peroxidase activity of thioredoxin reductase.

Muller et al is teaching that Ebselen is an enhancer of the peroxidase activity. See the title, column 1 of page 3235.

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the substrate of the thioredoxin reductase of Arteel et al for the enhancing of the peroxidase activity of the Muller et al, because the latter reference is expressly teaching that Ebselen is an enhancer of the peroxidase activity and the former reference teaching that the same Ebselen is the substrate for the thioredoxin reductase. Thus claimed subject matter is a prima facie obvious as a whole, absent evidence to the contrary.

**(11) Response to Argument**

Appellants admit that Arteel is directed to a study involving materials that are similar to those used in their process, at the same time, they disagree that Arteel does Not teach every element of the claimed invention. Appellants allege that Arteel does not teach any methods wherein ebselen is used as a substrate for thioredoxin reductase. Pointing to page 264, in the abstract, appellants allege that the addition of thioredoxin did not enhance "these' effects. Appellants further emphasizes that Arteel does perform experiment with ebselen, such as affinity of ebselen for thioredoxin reductase. On page 13, of the brief, top three lines, appellants quote, " thus, **the prior art at most teach that ebselen is an inhibitor of thioredoxin reductase, and that ebselen selenoxide can be a substrate, however, appellants' claims do not include selenoxide**".

Appellants on page 14 summarizes Arteel reference's action, and alleges that in the instant claims the substrate, such as ebselen, is a substrate for the thioredoxin reductase, not an inhibitor. On page 15, of the brief, lines 7-10, appellants point out to Arteel that "Ebselen has been shown previously to have an affinity for TR". On page 16, 1<sup>st</sup> paragraph, appellants point out that in the present invention, ebselen is a substrate being reduced by NADPH and thioredoxin reductase, and reduced ebselen is oxidized back to ebselen by hydrogen peroxide. Pages 17-20 of the brief, appellants point out to individual claims, and as to why the references do not anticipate them.

Appellants are claiming a method for reducing a substrate(in the present case it is ebselen) by combining with thioredoxin reductase and NADPH. The abstract of Arteel, is teaching that ebselen is functioning as substrate when combined with

Art Unit: 1621

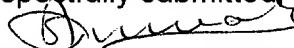
thioredoxin reductase and NADPH. Appellants point out that they are not claiming ebselen oxide, and the reference is teaching that ebselen oxide is reduced by NADPH and thioredoxin reductase. The reference on page 268, Figure 6, is the same method as claimed by the appellants. Also note, page 267, column 1, last paragraph, wherein it is expressly taught that ebselen is substrate. Also see Figure 4 on page 267. Appellants arguments that individual claims are directed to in vivo, and the reference is not teaching in-vivo is not convincing, inasmuch as the reference in the abstract is mentioning mammalian activity. Note, page 268, column 2, 1<sup>st</sup> paragraph, wherein ebselen is having affinity for TR.

With respect to arguments over obviousness rejection, appellants point out that mechanism by glutathione reductase is different than thioredoxin reductase. Appellants are not claiming mechanism, rather a method. Muller et al is expressly teaching that ebselen has glutathione peroxidase like activity, and is thus enhancer of peroxidase activity.

For the above reasons, it is believed that the rejections should be sustained.

Art Unit: 1621

Respectfully submitted,



SHAIENDRA - KUMAR

Primary Examiner

Art Unit 1621

S.Kumar

November 4, 2004

Conferees



Johann Richter (Supervisory Patent Examiner)



Deborah Carr (primary Examiner)

GREENBLUM & BERNSTEIN, P.L.C.  
1950 ROLAND CLARKE PLACE  
RESTON, VA 20191